

Appln. No.09/890,297
Suppl. Arndt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

Claims 1-53 (cancelled)

Claim 54 (previously added): A process for purifying an albumin solution, the process comprising

- (1) subjecting the albumin solution to cation exchange chromatography in the negative mode with respect to the albumin in order to yield an albumin-containing cation exchange product;
- (2) subjecting the albumin-containing cation exchange product, with or without intervening purification steps, to anion exchange chromatography to yield an albumin-containing anion exchange product; and
- (3) placing the albumin-containing anion exchange product, without further purification, into a final container for therapeutic use

Claim 55 (previously added): A process according to Claim 54 wherein the initial albumin solution contains glycosylated albumin and the glycosylated albumin is bound during the said cation exchange step.

Claim 56 (previously added): A process according to Claim 54 wherein the cation exchange step utilises a matrix which comprises immobilised sulfopropyl substituents as cation exchangers.

Claim 57 (previously added): A process according to Claim 54 wherein the initial albumin solution has a pH of 4.5-6.0.

Claim 58 (previously added): A process according to Claim 54 wherein the initial albumin solution has an albumin concentration of 10-250g.L⁻¹.

Appln. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

Claim 59 (previously added): A process according to Claim 54 wherein the initial albumin solution has an octanoate ion concentration of 2-15mM.

Claim 60 (previously added): A process according to Claim 54 wherein the initial albumin solution has an octanoate ion concentration of 5-10mM.

Claim 61 (previously added): A process according to Claim 54 wherein prior to the cation exchange step the albumin solution undergoes at least one step selected from the group consisting of: (i) pH-adjustment; (ii) concentration; (iii) diafiltration; and (iv) conditioning by addition of a fatty acid.

C
CD S/T.

Claim 62 (previously added): A process according to Claim 61 wherein prior to the cation exchange step the albumin solution undergoes conditioning by addition of an octanoate salt.

Claim 63 (previously added): A process according to Claim 54 wherein the anion exchange step utilises a matrix which comprises immobilised dialkylaminoalkyl substituents as anion exchangers.

Claim 64 (previously added): A process according to Claim 54 wherein the anion exchange step is run in the negative mode with respect to the albumin.

Claim 65 (previously added): A process according to Claim 64 wherein the albumin solution which undergoes anion exchange chromatography has a pH of 4.0-5.2.

Claim 66 (previously added): A process according to Claim 64 wherein the albumin solution which undergoes anion exchange chromatography has a conductivity of less than 4.0mS.cm⁻¹.

Claim 67 (previously added): A process according to Claim 54 wherein the anion exchange step is run in positive mode with respect to the albumin.

Appln. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

Claim 68 (previously added): A process according to Claim 67 wherein the albumin solution which undergoes positive mode anion exchange chromatography has a pH of 6.0-8.0.

Claim 69 (previously added): A process according to Claim 67 wherein the concentration of the albumin in the albumin solution which undergoes positive mode anion exchange chromatography is 10-100g.L⁻¹

Claim 70 (previously added): A process according to Claim 67 wherein the albumin solution which undergoes positive mode anion exchange chromatography has a conductivity of 1.0-1.5mS.cm⁻¹.

CL
CDJ+.

Claim 71 (previously added): A process according to Claim 67 wherein the albumin is eluted in the anion exchange step using a buffer comprising a compound having a specific affinity for albumin.

Claim 72 (previously added): A process according to Claim 71 wherein the buffer comprises 20-90mM phosphoric acid salt.

Claim 73 (previously added): A process according to Claim 67 wherein the albumin is eluted in the anion exchange step with a buffer of pH6.0-8.0.

Claim 74 (previously added): A process according to Claim 54 wherein, prior to the anion exchange step, the albumin solution undergoes at least one step selected from the group consisting of: buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; treatment with a reducing agent; decolouration treatment; heating; cooling; and conditioning

Claim 75 (previously added): A process according to Claim 54 wherein the process is preceded by at least one step selected from the group consisting of: fermentation; primary separation; concentration; conditioning; cation exchange chromatography; anion exchange chromatography, and affinity chromatography.

Appln. No.09/890,297
Suppl. Arndt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

Claim 76 (currently amended): A process for purifying an albumin solution, the process comprising

- (1) subjecting the albumin solution to cation exchange chromatography in the negative mode with respect to the albumin in order to yield an albumin-containing cation exchange product;
- (2) subjecting the albumin-containing cation exchange product, with or without intervening purification steps, to anion exchange chromatography to yield an albumin-containing anion exchange product; and
- (3) placing the albumin-containing anion exchange product, without further purification, into a final container for therapeutic use,

wherein the albumin-containing anion exchange product is subjected to at least one step selected from the group consisting of buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; treatment with a reducing agent; decoloration treatment; heating; cooling; and conditioning, before being placed into the said final container.

Claim 77 (previously added): A process according to Claim 76 wherein the initial albumin solution contains glycosylated albumin and the glycosylated albumin is bound during the said cation exchange step.

Claim 78 (previously added): A process according to Claim 76 wherein prior to the cation exchange step the albumin solution undergoes at least one step selected from the group consisting of: (i) pH-adjustment; (ii) concentration; (iii) diafiltration; and (iv) conditioning by addition of a fatty acid.

Claim 79 (currently amended): A process for purifying an albumin solution, the process comprising

- (1) subjecting the albumin solution to anion exchange chromatography in order to yield an albumin-containing anion exchange product;
- (2) subjecting the albumin-containing anion exchange product, with or without intervening purification steps, to cation exchange chromatography run in the negative mode with respect to the albumin to yield an albumin-containing cation exchange product; and

Appn. No.09/890,297
Suppl. Armdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

(3) placing the albumin-containing cation exchange product, without further purification, into a final container for therapeutic use, wherein the albumin-containing cation exchange product is subjected to at least one step selected from the group consisting of buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; treatment with a reducing agent; decoloration treatment; heating; cooling; and conditioning, before being placed into the said final container.

Claim 80 (previously added): A process according to Claim 79 wherein the initial albumin solution contains glycosylated albumin and the glycosylated albumin is bound during the said cation exchange step.

CL
CDT.

Claim 81 (previously added): A process according to Claim 79 wherein prior to the cation exchange step the albumin solution undergoes at least one step selected from the group consisting of: (i) pH-adjustment; (ii) concentration; (iii) diafiltration; and (iv) conditioning by addition of a fatty acid.

Claim 82 (previously added): A process for purifying an albumin solution, the process comprising the steps of:

- (i) subjecting an albumin solution to a cation exchange chromatography step run in positive mode with respect to the albumin;
- (ii) collecting an albumin-containing cation exchange eluate;
- (iii) subjecting the cation exchange eluate to an anion exchange chromatography step run in positive mode with respect to the albumin;
- (iv) collecting an albumin-containing anion exchange eluate;
- (v) subjecting the anion exchange eluate to an affinity chromatography step run in positive mode with respect to the albumin;
- (vi) collecting an albumin-containing affinity chromatography eluate;
- (vii) subjecting the affinity chromatography eluate to an affinity chromatography step run in negative mode with respect to the albumin and in positive mode with respect to glycoconjugates;
- (viii) collecting the albumin-containing affinity chromatography flow through;
- (ix) subjecting the affinity chromatography flow through to a cation exchange chromatography step run in negative mode with respect to the albumin;

Appln. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

- (x) collecting the albumin-containing cation exchange flow through;
- (xi) subjecting the cation exchange flow through to an anion exchange chromatography step run in negative mode; and
- (xii) collecting the albumin-containing anion exchange flow through from step (xi).

Claim 83 (previously added): A process for purifying an albumin solution, the process comprising the steps of:

- (i). subjecting an albumin solution to a cation exchange chromatography step run in positive mode with respect to the albumin;
- (ii). collecting an albumin-containing cation exchange eluate;
- (iii). subjecting the cation exchange eluate to an anion exchange chromatography step run in positive mode with respect to the albumin;
- (iv). collecting an albumin-containing anion exchange eluate;
- (v). subjecting the anion exchange eluate to an affinity chromatography step run in positive mode with respect to the albumin;
- (vi). collecting an albumin-containing affinity chromatography eluate;
- (vii). subjecting the affinity chromatography eluate to an affinity chromatography step run in negative mode with respect to the albumin and in positive mode with respect to glycoconjugates;
- (viii). collecting the albumin-containing affinity chromatography flow through;
- (ix). subjecting the affinity chromatography flow through to a cation exchange chromatography step run in negative mode with respect to the albumin;
- (x). collecting the albumin-containing cation exchange flow through;
- (xi). subjecting the cation exchange flow through to an anion exchange chromatography step run in positive mode; and
- (xii). eluting from the anion exchange matrix an anion exchange eluate.

Claim 84 (previously added): A process according to Claim 82 wherein any of the said purification steps are optionally preceded or followed by at least one step selected from the group consisting of: buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; treatment with a reducing agent; decolouration treatment; heating; cooling; and conditioning.

Appn. No.09/890,297
Suppl. Amdt. Dat d May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

Claim 85 (previously added): A process according to Claim 83 wherein any of the said purification steps are optionally preceded or followed by at least one step selected from the group consisting of: buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; treatment with a reducing agent; decolouration treatment; heating; cooling; and conditioning.

Claim 86 (previously added): A process for purifying an albumin solution, the process comprising the steps of:

CI
CDD:t

- (i) subjecting an albumin solution to a cation exchange chromatography step run in positive mode with respect to the albumin;
- (ii) collecting an albumin-containing cation exchange eluate;
- (iii) subjecting the cation exchange eluate to an anion exchange chromatography step run in positive mode with respect to the albumin;
- (iv) collecting an albumin-containing anion exchange eluate;
- (v) subjecting the anion exchange eluate to an affinity chromatography step run in positive mode with respect to the albumin;
- (vi) collecting an albumin-containing affinity chromatography eluate;
- (vii) subjecting the affinity chromatography eluate to an affinity chromatography step run in negative mode with respect to the albumin and in positive mode with respect to glycoconjugates;
- (viii) collecting the albumin-containing affinity chromatography flow through;
- (ix) subjecting the affinity matrix flow through to an anion exchange chromatography step run in negative mode with respect to the albumin;
- (x) collecting the albumin-containing anion exchange flow through from step (ix);
- (xi) subjecting the albumin solution purified by the anion exchange chromatography step to a cation exchange chromatography step run in negative mode with respect to the albumin; and
- (xii) collecting the albumin-containing cation exchange flow through.

Claim 87 (previously added): A process for purifying an albumin solution, the process comprising the steps of:

- (i). subjecting an albumin solution to a cation exchange chromatography step run in positive mode with respect to the albumin;

Appn. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

(ii). collecting an albumin-containing cation exchange eluate;

(iii). subjecting the cation exchange eluate to an anion exchange chromatography step run in positive mode with respect to the albumin;

(iv). collecting an albumin-containing anion exchange eluate;

(v). subjecting the anion exchange eluate to an affinity chromatography step run in positive mode with respect to the albumin;

(vi). collecting an albumin-containing affinity chromatography eluate;

(vii). subjecting the affinity chromatography eluate to an affinity chromatography step run in negative mode with respect to the albumin and in positive mode with respect to glycoconjugates;

(viii). collecting the albumin-containing affinity chromatography flow through;

(ix). subjecting the affinity matrix flow through to an anion exchange chromatography step run in positive mode with respect to the albumin;

(x). eluting from the anion exchange matrix an anion exchange eluate;

(xi). subjecting the albumin solution purified by the anion exchange chromatography step to a cation exchange chromatography step run in negative mode with respect to the albumin; and

(xii). collecting the albumin-containing cation exchange flow through.

Claim 88 (previously added): A process according to Claim 86 wherein any of the said purification steps are optionally preceded or followed by at least one step selected from the group consisting of: buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; addition of reducing agent; decolouration treatment; heating; cooling; and conditioning.

Claim 89 (previously added): A process according to Claim 87 wherein any of the said purification steps are optionally preceded or followed by at least one step selected from the group consisting of: buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; addition of reducing agent; decolouration treatment; heating; cooling; and conditioning.

Claim 90 (previously added): A process for purifying an albumin solution, the process comprising

(1) subjecting the albumin solution to anion exchange chromatography in order to

Appln. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

yield an albumin-containing anion exchange product;

(2) subjecting the albumin-containing anion exchange product, with or without intervening purification steps, to cation exchange chromatography run in the negative mode with respect to the albumin to yield an albumin-containing cation exchange product; and

(3) placing the albumin-containing cation exchange product, without further purification, into a final container for therapeutic use.

Claim 91 (previously added): A process according to Claim 90 wherein the initial albumin solution contains glycosylated albumin and the glycosylated albumin is bound during the said cation exchange step

C1
CDD4.

Claim 92 (previously added): A process according to Claim 90 wherein the cation exchange step utilises a matrix which comprises immobilised sulfopropyl substituents as cation exchangers.

Claim 93 (previously added): A process according to Claim 90 wherein the albumin solution that undergoes cation exchange chromatography has a pH of 4.5-6.0

Claim 94 (previously added): A process according to Claim 90 wherein the albumin solution that undergoes cation exchange chromatography has an albumin concentration of 10-250g.L⁻¹.

Claim 95 (previously added): A process according to Claim 90 wherein the albumin solution that undergoes cation exchange chromatography has an octanoate ion concentration of 2-15mM.

Claim 96 (previously added): A process according to Claim 90 wherein prior to the cation exchange step the albumin solution undergoes at least one step selected from the group consisting of: (i) pH adjustment; (ii) concentration; (iii) diafiltration; and (iv) conditioning by addition of a fatty acid.

Appn. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

Claim 97 (previously added): A process according to Claim 96 wherein prior to the cation exchange step the albumin solution undergoes conditioning by addition of an octanoate salt.

Claim 98 (previously added): A process according to Claim 90 wherein the anion exchange step utilises a matrix which comprises immobilised dialkylaminoalkyl substituents as anion exchangers.

Claim 99 (previously added): A process according to Claim 90 wherein the anion exchange step is run in the negative mode with respect to the albumin.

Claim 100 (previously added): A process according to Claim 99 wherein the albumin solution which undergoes anion exchange chromatography has a pH of 4.0-5.2.

Claim 101 (previously added): A process according to Claim 99 wherein the albumin solution which undergoes anion exchange chromatography has a conductivity of less than 4.0mS.cm⁻¹.

Claim 102 (previously added): A process according to Claim 90 wherein the anion exchange step is run in positive mode with respect to the albumin

Claim 103 (previously added): A process according to Claim 102 wherein the albumin solution which undergoes positive mode anion exchange chromatography has a pH of 6.0-8.0.

Claim 104 (previously added): A process according to Claim 102 wherein the concentration of the albumin in the albumin solution which undergoes positive mode anion exchange chromatography is 10-100g.L⁻¹

Claim 105 (previously added): A process according to Claim 102 wherein the albumin solution which undergoes positive mode anion exchange chromatography has a conductivity of 1.0-1.5mS.cm⁻¹.

Appln. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

Claim 106 (previously added): A process according to Claim 102 wherein the albumin is eluted in the anion exchange step using a buffer comprising a compound having a specific affinity for albumin.

Claim 107 (previously added): A process according to Claim 106 wherein the buffer comprises 20-90mM phosphoric acid salt.

Claim 108 (previously added): A process according to Claim 102 wherein the albumin is eluted in the anion exchange step with a buffer of pH6.0-8.0.

Claim 109 (previously added): A process according to Claim 90 wherein, prior to the cation exchange step, the albumin solution undergoes at least one step selected from the group consisting of: buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; treatment with a reducing agent; decolouration treatment; heating; cooling; and conditioning.

C 1
CDT.

Claim 110 (currently amended): A process according to Claim 90 wherein the process is preceded by at least one step selected from the group consisting of: fermentation; primary separation; ~~concentration~~; centrate conditioning; cation exchange chromatography; anion exchange; and affinity chromatography.

Claim 111 (previously added): A process for purifying an albumin solution, the process comprising

- (1) subjecting the albumin solution to anion exchange chromatography in order to yield an albumin-containing anion exchange product;
- (2) subjecting the albumin-containing anion exchange product, with or without intervening purification steps, to cation exchange chromatography run in the negative mode with respect to the albumin to yield an albumin-containing cation exchange product; and
- (3) placing the albumin-containing cation exchange product, without further purification, into a final container for therapeutic use,

wherein, prior to the cation exchange step, the albumin solution undergoes at least one step selected from the group consisting of: buffer exchange; concentration; dilution; dialysis; diafiltration; pH-adjustment; treatment with a reducing agent; decolouration

Appn. No.09/890,297
Suppl. Amdt. Dated May 19, 2003
Reply to Office action of February 20, 2003

Attorney File No.: CE0253 US

treatment; heating; cooling; and conditioning.

(C)

Claim 112 (previously added): A process according to Claim 111 wherein the initial albumin solution contains glycosylated albumin and the glycosylated albumin is bound during the said cation exchange step.

CDT.

Claim 113 (previously added): A process according to Claim 111 wherein prior to the cation exchange step the albumin solution undergoes at least one step selected from the group consisting of: (i) pH-adjustment; (ii) concentration; (iii) diafiltration; and (iv) conditioning by addition of a fatty acid.